

REMARKS**RECEIVED
CENTRAL FAX CENTER****NOV 27 2006****Summary of the Office Action**

Claims 1-10, 12-17, and 23-27 were pending and have been examined. The Examiner contends that dependent claims 9, 14, and 16 are directed to unelected subject matter, and hence has withdrawn these claims.

Claims 24, 26, and 27 are rejected under 35 U.S.C. § 112, paragraph 1. Claims 1, 2-7, 17, 23, 24, and 27 are rejected under 35 U.S.C. § 112, paragraph 2.

Claims 1, 5-8, 10, 13, 15, and 23-27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Freskos (U.S. Patent 6,143,747). Claims 1, 5, 6, 8, 10, 13, 15, and 23-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Freskos.

Claims 1-8, 15, and 23-27 are objected to as being directed to non-elected subject matter.

Applicants appreciate the Examiner's statement that claim 12 would be allowable if rewritten in independent form.

All of these rejections are traversed.

Amendments to the Claims

Claims 1-7, 10, 17, 23, 26, and 27 have been amended herein. Claim 8 is canceled herein without prejudice. Claims 28-31 have been newly added.

Claim 1 has been amended, *inter alia*, to amend the definitions of E', B, G, D, and R⁷ in order to exclude non-elected subject matter. In view of the amended definition of E' in claim 1, claim 8 has been canceled without prejudice.

Claims 2-4 have been amended to make clear that the D' substituent (which is selected from C₁-C₁₅ alkyl, C₂-C₁₅ alkenyl or C₂-C₁₅ alkynyl) is optionally substituted with C₃-C₈ cycloalkyl.

Claim 1 has also been amended, *inter alia*, with respect to the definition of D'. Specifically, "halo," "-SR³," "-N(R³)₂," and "-S(O)_n-R³," have been excluded as possible substituents of D'. In addition, a proviso in the definition of D' has been canceled. Dependent claims 5-7 have been amended in a corresponding manner to conform to these amendments of claim 1.

Claim 17 has been amended to include the structures that correspond to the recited compound numbers.

Claim 23 has been amended to more particularly point out and distinctly claim the subject matter of applicants' invention, as well as to remove dependencies to withdrawn and canceled claims. Claim 27 has been amended for clarity.

Claim 10 has been amended to depend from claim 1. Claim 26 has been amended to depend only from claim 23. Claims 28-31 have been newly added as methods of administering the compositions of their respective parent claims 24 and 25.

Applicants submit that these amendments are fully supported by the specification and claims as originally filed, and do not introduce any new matter. Entry of these amendments is respectfully requested.

Claims 1-7, 10, 12, 13, 15, 17, and 23-31 therefore remain in this application for further examination.

Non-Elected Subject Matter

Claims 1-8, 15, and 23-27 are objected to for allegedly containing non-elected subject matter. Solely to advance prosecution of this application to allowance, applicants have

amended claim 1 with respect to the definitions of substituents E', B, G, D, and R⁷, such that claim 1 is directed to the compounds represented in Table 1 of the specification. Dependent claims 2-7, 15, and 23-27 are likewise directed for at least the same reasons. Reconsideration and withdrawal of this objection is therefore requested.

Rejections Under 35 U.S.C. § 112

I. Enablement (Claims 24, 26, and 27)

Claims 24, 26, and 27 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. Applicants disagree with this rejection for at least the following reasons.

Claims 24, 26, and 27 are directed to compositions comprising a compound of the present invention or a pharmaceutically acceptable salt thereof, and "an additional antiviral agent." The Examiner contends that this claim would not have been enabled because there is no teaching in the specification "regarding using instant compounds in combination with any other agent." (Office Action at page 3.) Applicant respectfully disagrees, as such knowledge was already well-known in the art. For example, applicants' specification makes clear that the compounds of the present invention "can be used alone or in combination with other therapeutic or prophylactic agents, such as anti-virals . . . for the treatment or prophylaxis of viral infection." (Specification at page 3, lines 26-30.) For example, the instant compounds may be administered "in combination with other anti-viral agents which interfere with the replication cycle of HIV." (*Id.* at page 74, lines 27-30.) The use of such combination antiviral therapies, particularly for treatment or prophylaxis of HIV, was well-known known to result in certain advantages, such as the potentiation of the compounds' therapeutic effects and other synergistic effects, reduced dosage requirements, reduced side effects and toxicity, and other advantages that were known to persons skilled in the art. (See, e.g., specification at page 75, lines 1-2 and at page 87, line 18 to page 88, line 7.) Therefore, applicants submit that compositions of combinations of anti-viral compounds would have been well-known to a person of ordinary skill in the art.

The Examiner also contends that there is no teaching in the specification "regarding mechanism of action of other antiviral agents for antiviral activity." Applicants disagree with this contention as well, as many anti-viral agents and their mechanisms of action would have been well-known in the art. Examples of such anti-viral agents that may be used in combination with the compounds of the present invention are listed in applicants' specification at page 75, lines 2-17, and at page 88, line 1 to page 89, line 12. Moreover, the mechanisms of action of these and other agents were also known to those of ordinary skill in the art. Examples of mechanisms included interfering with "cell entry, reverse transcription and viral DNA integration into cellular DNA." (*Id.* at page 75, lines 2-6.)

Finally, the Examiner contends that the specification lacks working examples because the outcome of combination treatment entailed a "lot of speculation and unpredictability." (Office Action at page 3.) Applicants disagree that any undue experimentation would have been required. As acknowledged by the Examiner, the specification provides ample support for suitable assays for measuring the efficacy of antiviral agents, such as the MT4 cell-based assays at pages 348-353. Thus, in view of the well-known applications and advantages of combination antiviral therapies, a person of ordinary skill in the art could have use these and like assays to test combinations of antiviral agents. Indeed, such numerically large-scale assays are well-known and routine in this art, and thus would not have required undue experimentation.

Therefore, for at least the reasons presented above, applicants submit that all of the Examiner's contentions underlying the lack of enablement rejection are either incorrect or unsupported. Accordingly, applicants respectfully request reconsideration and withdrawal of this rejection.

II. Indefiniteness (Claims 1-7, 17, and 23)

Claims 1-7, 17, and 23 are rejected under 35 U.S.C. § 112, second paragraph, for being allegedly indefinite. Applicants traverse these rejections. However, for the sole

reason to advance prosecution of this application to allowance, applicants have obviated these rejections by amending these claims in the manner described below:

A) Claims 1 and 5-7 are rejected because of the proviso in the definition of substituent D' which recites, *inter alia*, "when R¹ is -C(O)-." The Examiner states that this proviso is invalid because R¹ has been previously defined as -O-C(O)-. Applicants have obviated this rejection by canceling this proviso in claims 1 and 5-7.

B) Claims 2-4 are rejected because it is alleged that it is unclear what is being referenced by the term "each of which is optionally substituted C₃-C₈ cycloalkyl." To obviate this rejection, applicants have amended claims 2-4 to make more clear that this term refers to the D' substituent, and not to the -CN groups thereon.

C) Claim 17 is rejected because structures corresponding to the recited compound numbers are missing. Accordingly, applicants have amended this claim to include structures for all of the recited compound numbers.

D) Claim 23 is rejected because the term "detectably inhibit protease activity in a patient" is allegedly vague and indefinite. Applicants disagree, but nonetheless have amended this claim in the manner suggested by the Examiner, thereby obviating this rejection.

In view of the above-described amendments, applicants requests reconsideration and withdrawal of these rejections under 35 U.S.C. § 112.

III. Indefiniteness (Claims 24 and 27)

Claims 24 and 27 are rejected because the term "additional antiviral agent" is allegedly indefinite because a "specific agent with defined structure is not defined." (Office Action at page 5.) Applicants disagree with this requirement, and instead submits that these

claims fully satisfy the requirements of 35 U.S.C. § 112, second paragraph, for at least the following reasons.

First, "antiviral agents" is a term that would have been well-understood by a person having ordinary skill in the art. Second, this term is also defined in the specification. (See, e.g., page 2, line 19 to page 3, line 21; and page 74, line 27 to page 75, line 17.) Third, specific examples of anti-viral agents are also provided in the specification. (See, e.g., page 75, lines 2-17, and page 88, line 1 to page 89, line 12.) For at least these reasons, applicants submit that the scope of these claims would have been "clear to a hypothetical person possessing the ordinary level of skill in the pertinent art" (MPEP § 2171).

In addition, applicants have amended claim 26 to depend only from claim 23. Thus, dependent claim 27 makes clear that the additional antiviral agent is being administered prior to, simultaneously with or following administration of a composition comprising a compound of the present invention.

In view of the above, applicants request reconsideration and withdrawal of these rejections under 35 U.S.C. § 112.

Rejections Under 35 U.S.C. § 102(e)

Claims 1, 5-8, 10, 13, 15, and 23-27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Freskos. Specifically, the Examiner contends that these claims are anticipated by compounds 34, 37, and 38 in Table 1A, column 41 of Freskos. Applicants traverse this rejection.

Nonetheless, to advance prosecution of this applications to allowance, applicants have amended claim 1 such that the definition of D' no longer recites " $-SR^3$," " $-N(R^3)_2$," and " $-S(O)_n-R^3$," as a possible substituents of D'. Applicants therefore submit that amended claim 1 is not anticipated by Freskos. Claims 5-7, 10, 13, 15, and 23-29, which depend from claim 1, are also not anticipated by Freskos for at least the same reasons. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 1, 5, 6, 8, 10, 13, 15, and 23-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Freskos. In particular, the Examiner cites compounds 12, 14, 36, 48, and 49 in Table 1A at columns 40-42 of Freskos, but acknowledges that these compounds differ from applicants' claimed compounds because Freskos's compounds have "unsubstituted alkyl groups instead of [alkyl groups] substituted with halogen" at the position corresponding to D' of applicants' Formula I. However, the Examiner contends that "the generic teachings of Freskos teach that [the position corresponding to D'] can also be a haloalkyl." (Office Action at page 6.) Based on these contentions, the Examiner contends that Freskos renders these claims unpatentable. Applicants traverse this rejection.

Nonetheless, to advance prosecution of this applications to allowance, applicants have amended claim 1 such that the definition of D' no longer recites "halo" as a possible substituent of the D' substituent. In view of this amendment, applicants submit that, even assuming that the Examiner's characterization of Freskos were correct, it would not have been obvious to prepare the claimed compounds of amended claim 1 based on the compounds referenced in Freskos. For at least this reason, applicants submit that amended claim 1 would not have been rendered obvious in view of Freskos. Claims 5, 6, 10, 13, 15, and 23-29, which depend from claim 1, also would not have been rendered obvious in view of Freskos for at least the same reasons. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

RECEIVED
CENTRAL FAX CENTER
NOV 27 2006

Conclusion

Applicants request favorable consideration of the application and early allowance of the pending claims. Should the Examiner feel that a telephone conference with applicants' representatives would assist the Examiner, he is invited to telephone the undersigned at anytime.

Respectfully submitted,



James F. Haley, Jr. (Reg. No. 27,794)
Karen Mangasarian (Reg. No. 43,772)
Attorneys for Applicants

Tac Bum Shin (Ltd. Reg. No. L0091)
Agent for Applicants

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
Customer No. 1473
1251 Avenue of the Americas
New York, New York 10020-1105
Tel.: (650) 617-4000 (CA)
Fax: (212) 596-9090 (NY)